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Editors Welcome

Changes in patient and physician attitudes resulting from COVID-19 in neuromyelitis optica spectrum disorder and multiple sclerosis

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At the onset of the pandemic, immunosuppression was a suspected risk factor for COVID-19. However, we still do not have data to support or refute this concern. Meanwhile, patients and their doctors are questioning whether they should lighten the immunosuppressive regimen to improve patients' immunological defenses against the virus.

Two of us (SS and ML) explored the impact of this concern in a poll of 186 randomly selected patients with neuromyelitis optica spectrum disorder on a closed Facebook group. We asked about their perspective on their current treatment and whether their health care providers influenced treatment decisions during the pandemic. As expected, the most frequent concern was acquiring the infection (80.6%). There were also anxieties about spreading the infection inadvertently (16.1%) and worries about the economic downturn (9.7%), as well as social isolation (9.1%). The most commonly used medications in this population were: rituximab (66.7%), mycophenolate mofetil (14%), corticosteroids (12%), azathioprine (6.4%), eculizumab (4.8%), and tocilizumab (2%). When asked about changing their medications, 85% patients had never considered stopping treatment. A small number delayed their rituximab infusion on the advice of their treating physicians. Reassuringly, the majority remained in contact with their medical advisers. In 31%, contact was through personal clinic visits, while in the remaining it was remote: email/phone (28.5%), telemedicine (26.9%), or no contact (13.6%). From this poll, it appears that most NMO patients did not change or stop their medication despite concerns that they might acquire COVID-19.

In this issue of Multiple Sclerosis and Related Disorders (MSARD), there are several case reports relating to the impact of immunosuppressive therapy on COVID-19 outcomes in multiple sclerosis and related disorders. One paper describes a 57-year-old female with MS who developed severe Covid -19 infection (Foerch et al 2020). The Extended Disability Status Scale (EDSS) was 2.0 indicating low baseline disability. There was longstanding lymphopenia presumably resulting from 9 years of treatment with fingolimod, a sphingosine-1-phosphate agonist. She experienced severe COVID-19 infection requiring non-invasive ventilation that improved within a few days to complete recovery. The helpful effect of sphingosine-1-phosphate to stabilize the pulmonary endothelial membrane and reduce of vascular permeability in alveoli may be the mechanism whereby fingolimod treatment led to good outcome in this case. They suggest fingolimod might also combat the cytokine storm reported in severe cases of COVID-19. The second fingolimod-treated MS patient was a 58-year-old female with more severe baseline disability (EDSS 6) who had been on treatment for 9 years (Valencia-Sanchez and Wingerchuk, 2020). Comorbidities included diabetes, hypertension, hyperlipidemia and transient ischemic attacks. The COVID-19 infection was serious, requiring intubation, mechanical ventilation and hemodynamic support. Tocilizumab was introduced, followed by gradual recovery over the next 10 days. The authors emphasize the value of tocilizumab, an interleukin-6 receptor (IL-6 R) blocker, in preventing the cytokine storm and its potential therapeutic benefits in end stage COVID-19, and was recently demonstrated (Colaneri et al., 2020; Xu et al., 2020).

Also, in this issue of MSARD are two separate reports concerning MS patients with COVID-19 who were taking ocrelizumab. The first article refers to a 58-year-old male who developed moderate hypogammaglobulinemia from long standing ocrelizumab-induced depletion of B cells followed by mild COVID-19 (Novi et al., 2020). His-symptoms resolved in 2 days prompting the authors to speculate that the persistence of B cells in the secondary lymphoid organs, along with a reduced immune response caused by the lack of peripheral B cells, might have been protective. Again, this could have weakened the effect of a potential COVID-19 cytokine storm. A second report from Spain (Montero-Escribano et al., 2020) analyzed the frequency and severity of COVID-19 in 9 patients exposed to anti-CD20 agents: 2 were on ocrelizumab and 7 were on rituximab. They concluded that these drugs do not play an important role in elevating the risk of infection by SARS-CoV2. The obvious limitations in this series are the small numbers and lack of viral testing in the majority of cases. Larger case series of the effect of B cell therapy in COVID-19 have been published recently as well (Giovannoni et al., 2020; Sormani and Italian Study Group, 2020).

Finally, we highlight an article from Poland where the authors used a questionnaire to assess the severity of COVID-19 in 22 patients suffering from either Parkinson's disease, MS or dementia all of whom were receiving adamantanes – namely amantadine or memantine (Rejdak and Grieb, 2020). Although their infection was confirmed by

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PCR testing and there was prior person-to -person contact with COVID-19 infected subjects (also verified by PCR testing), none developed symptoms. Adamantanes are thought to act by downregulating cathepsins and disrupting lysosomal pathways essential for viral replication. The authors suggested that adamantanes might have a role in lessening viral infectivity resulting in a better clinical outcome.

The current COVID-19 pandemic presents formidable challenges for neurologists when treating patients with immunosuppressive drugs. So far, concerns about these medications are mostly theoretical, based on their suspected mechanisms of action. Furthermore, we should be alert to the natural tendency for clinicians to report small numbers of patients taking major immunosuppressive treatment who unexpectedly do well when infected with COVID-19. Until more data are available, there needs to be a careful balance between the requirement for a potent drug to control disease activity and its safety profile. The provisional message from the manuscripts in this issue is that commonly used immunosuppressive therapies are generally safe to continue.

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